American Journal of Ophthalmology Case Reports 25 (2022) 101369

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

An intracameral approach for recalcitrant fungal keratitis

Libing K. Dong, David B. Krebs *

Central Michigan University College of Medicine, Saginaw, MI, USA

ARTICLE INFO

Keywords:
Fungal keratitis
Intracameral injection
Amphotericin B

ABSTRACT

Purpose: To describe 2 cases of recalcitrant fungal keratitis successfully treated with intracameral Amphotericin B.

Methods: Interventional case series.

Results: A 59-year-old female and a 41-year-old male each presented with fungal keratitis, caused by *Bipolaris* spp. and *Fusarium* spp. respectively. Both cases were unresponsive to topical antifungals, causing persistent discomfort and decreased vision. The two patients subsequently received a single dose of intracameral amphotericin B (ICAMB) 10mcg/0.1 mL, in addition to continued topical natamycin. Both patients had remarkable results following ICAMB, with best corrected visual acuity of 20/20 and full corneal reepithelization following treatment.

Conclusions: We report 2 cases of intractable fungal keratitis that benefited from intracameral injections of amphotericin B. This route of delivery appears to be very effective because the medication is delivered directly to the deeper layers of the cornea, where fungal infections tend to reside, and where topical and systemic routes have difficulty accessing.

1. Introduction

Fungal Keratitis is a serious and potentially sight threatening infection that accounts for up to 45% of all corneal infections worldwide.[1] The rate of infection varies by geographical location and socioeconomical class, with increased occurrences in marginalized populations and warmer/tropical climates.[2] A unique and problematic aspect of mycotic (vs. bacterial) keratitis is the ability of fungi to penetrate through deeper layers of the stroma and Descemet's membrane, resulting in a higher incidence of corneal perforation and endophthalmitis. While topical antifungal drops are the current standard of care, their limited stromal penetration have resulted in limited success in treating fungal keratitis.[3]

In this paper, we present two cases of intractable fungal keratitis successfully treated with intracameral injections of amphotericin B (ICAMB).

2. Findings

2.1. Case 1

A 59-year-old female with a history of soft contact lens wear was referred to us with complaints of pain, foreign body sensation, and decreased vision in her right eye. She had initially seen an optometrist two days prior and was placed on topical gatifloxacin (0.5%) and prednisolone acetate (1%) four times a day. The patient had no history of ocular trauma, past ocular or systemic disease, but frequently slept with her contact lenses. Examination revealed best corrected visual acuity (BCVA) of 20/400 in the right eye. Slit lamp examination showed a large corneal stromal infiltrate extending 60–70% in depth in the inferotemporal quadrant, with a 2.5mm × 3mm overlying epithelial defect, mild stromal thinning, and mild surrounding stromal edema. The anterior chamber had moderate cell and flare, as well as a 10% hypopyon. An endothelial plaque was not visualized. Fundus exam was unremarkable. Corneal scrapings were sent to be grown on blood agar, chocolate agar, and Sabouraud agar, and resulted in growth of *Bipolaris species*. The patient was placed on topical natamycin 5% hourly, topical voriconazole 1% hourly, and oral voriconazole 100mg twice daily. Over the course of the next five weeks, despite resolution of the hypopyon, no improvement was noted in the infiltrate (Fig. 1) and the patient developed severe, intractable pain.

Before performing a therapeutic penetrating keratoplasty, we decided to administer an injection of intracameral amphotericin B in the office. The concentration of amphotericin B used was 10mcg/0.1 mL,

* Corresponding author. Envision Eye Care, 5310 Hampton Place Suite 2, Saginaw, MI, 48604, USA.
E-mail address: dkrebs@chartermi.net (D.B. Krebs).

https://doi.org/10.1016/j.ajoc.2022.101369
Received 15 April 2020; Received in revised form 23 January 2022; Accepted 24 January 2022
Available online 27 January 2022

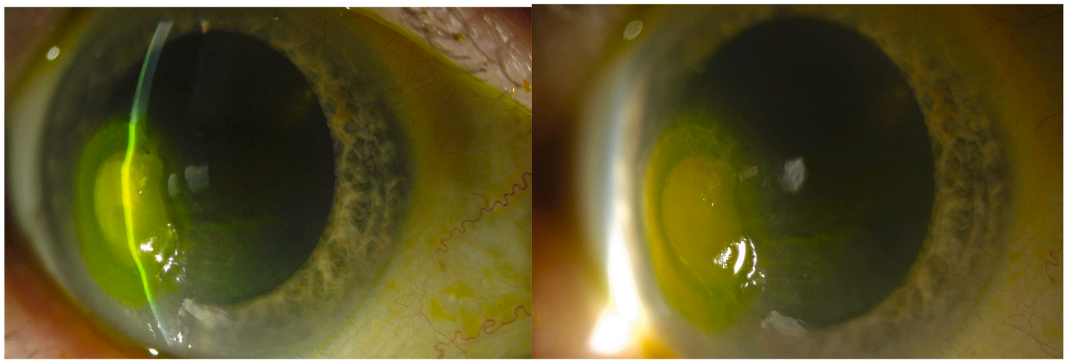

Fig. 1. Clinical appearance of case 1 seen on slit lamp following topical and oral antifungal treatment, but prior to intracameral amphotericin B. A persistent, white, ovoid shaped corneal infiltrate located at the 7 o'clock position.

same as that used in Yoon et el.[4] After administering topical tetracaine (0.5%), ofloxacin (0.3%), and betadine (5%), a 0.8mm self-sealing limbal paracentesis was made with a sterile superblade, and 0.1mL of amphotericin B (10mcg/0.1ml) was injected into the anterior chamber. Treatment with topical natamycin, topical and oral voriconazole was continued.

One day following the injection, the patient developed a small (3–5%) hypopyon. Three days later, the hypopyon resolved and the corneal infiltrate decreased in size. One week after injection, her vision improved to 20/60 and her pain had resolved. Three weeks after injection, the epithelium was intact and a mild stromal scar remained. Four weeks after injection, her vision improved to 20/20.

2.2. Case 2

A 41-year-old male with history of soft contact wear presented to us with a one-week complaint of pain, redness, and photophobia in his right eye. He had no past medical or ocular history but recalled an incident a few days prior in which he fell off his dirt bike into some swampy, muddy water. He also frequently slept in his contact lenses and used well water at home. He had been treated by his optometrist with frequent topical tobramycin (0.3%)/dexamethasone (0.1%) and besifloxacin (0.6%) for one week without improvement.

Examination revealed a BCVA of hand motions in the right eye. Slit lamp examination revealed a corneal stromal infiltrate extending 70% in depth, with a 2.5mm × 2.5mm overlying epithelial defect in the inferotemporal quadrant. Some keratic precipitates were present. The anterior chamber had moderate cell and flare, and a 5–10% hypopyon. Fundus exam showed no evidence of endophthalmitis. Corneal scrapings were obtained and plated on blood agar, chocolate agar, and Sabouraud agar. He was started on hourly topical polymyxin B sulfate (10,000 units/mL)/trimethoprim sulfate (1mg/mL) and topical polyhexamethylene biguanide (0.2mg/mL). Cultures revealed *Fusarium species*. The patient was subsequently switched to topical natamycin 5% every hour. Oral voriconazole was recommended, but patient declined due to cost. Three weeks later, the hypopyon had resolved but the infiltrate persisted with no improvement, vision remained hand motions and he developed severe pain and photophobia. At that time, we administered an injection of intracameral amphotericin B (10mcg/0.1 mL) using the same technique as in patient 1. Treatment with topical natamycin was continued. One week after injection, the epithelial defect and stromal infiltrate had decreased in size, BCVA improved to 20/70, and he noted less pain. One month after injection, examination showed total reepithelialization of the cornea, a residual stromal scar, and BCVA of 20/30. Three months later, vision was 20/20 with spectacles.

3. Discussion

Fungal keratitis remains a significant cause of corneal morbidity due to the ability of fungi to penetrate deep into the posterior cornea and anterior chamber, and limited penetration of topical antifungal agents. Systemic routes have poor bioavailability into the anterior chamber and may have serious systemic side effects.[5,6] Additionally, as seen in the MUTT II study, oral voriconazole is not helpful in cases of severe fungal keratitis.[7,8] Subconjunctival injections have limited penetration into the anterior chamber, and have adverse effects such as persistent periocular inflammation, epithelial ulcerations, and even tissue necrosis.[9] Intrastromal injections of antifungals have not been shown to be more effective than topical treatments.[10] Lastly, penetrating keratoplasties are invasive, risky, and performed as a last resort.

In each of our cases, the patients had a deep stromal infiltrate that did not respond to prolonged aggressive topical antifungal therapy but resolved promptly after a single intracameral injection of amphotericin B.

Previous reports have demonstrated effectiveness of intracameral administration of antifungals for fungal keratitis. Yoon et el[4] demonstrated that intracameral amphotericin B (ICAMB) is effective in reducing the time of hypopyon resolution and improving final outcomes. Shao et el[11] showed that ICAMB injection leads to faster healing time and resolution of hypopyon compared with topical amphotericin B. Sharma et el[10] demonstrated that ICAMB can be safely administered to improve healing of the cornea and prevent the progression of ulcers, with no complications in more than 80% of patients. Observational adverse effects of ICAMB were mostly limited to post injection pain and discomfort, typically resolved within hours. Other potential complications may include anterior chamber reaction, transient hypopyon formation, secondary infection through the keratolimbal paracentesis, bleeding from mechanical trauma to the iris, and formation of anterior subcapsular cataract in the unlikely event that the needle comes in contact with the anterior lens capsule.[12] Although intracameral antifungal injections have been reported for fungal keratitis, this treatment may not be well known amongst many ophthalmologists and cornea specialists.

In conclusion, we believe that intracameral amphotericin B should be considered for deep corneal fungal infections which are recalcitrant to aggressive topical antifungal therapy.

References

[1]. Niu L, Liu X, Ma Z, et al. Fungal keratitis: pathogenesis, diagnosis and prevention. *Microb Pathog.* 2020 Jan;138:103802.
[2]. Austin A, Lietman T, Rose-Nussbaumer J. Update on the management of infectious keratitis. *Ophthalmology.* 2017 Nov;124(11):1678–1689.
[3]. Ansari Z, Miller D, Galor A. Current thoughts in fungal keratitis: diagnosis and treatment. *Curr. Fungal. Infect. Rep.* 2013 Sep 1;7(3):209–218.
[4]. Yoon K-C, Jeong I-Y, Im S-K, Chae H-J, Yang S-Y. Therapeutic effect of intracameral amphotericin B injection in the treatment of fungal keratitis. *Cornea.* 2007 Aug;26(7):814–818.
[5]. Sahay P, Singhal D, Nagpal R, et al. Pharmacologic therapy of mycotic keratitis. *Surv Ophthalmol.* 2019 Jun;64(3):380–400.

[6]. Green WR, Bennett JE, Goos RD. Ocular penetration OF amphotericin B: a report OF laboratory studies and a case report OF postsurgical cephalosporium endophthalmitis. *Arch Ophthalmol*. 1965 Jun;73:769–775.
[7]. Prajna NV, Krishnan T, Rajaraman R, et al. Effect of oral voriconazole on fungal keratitis in the mycotic ulcer treatment trial II (MUTT II): a randomized clinical trial. *JAMA Ophthalmol*. 2016 Dec 1;134(12):1365–1372.
[8]. Schein OD. Evidence-based treatment of fungal keratitis. *JAMA Ophthalmol*. 2016 Dec 1;134(12):1372–1373.
[9]. Isipradit S. Efficacy of fluconazole subconjunctival injection as adjunctive therapy for severe recalcitrant fungal corneal ulcer. *J Med Assoc Thai*. 2008 Mar;91(3): 309–315.
[10]. Sharma N, Chacko J, Velpandian T, et al. Comparative evaluation of topical versus intrastromal voriconazole as an adjunct to natamycin in recalcitrant fungal keratitis. *Ophthalmology*. 2013 Apr;120(4):677–681.
[11]. Shao Y, Yu Y, Pei C-G, et al. Therapeutic efficacy of intracameral amphotericin B injection for 60 patients with keratomycosis. *Int J Ophthalmol*. 2010;3(3):257–260.
[12]. Kuriakose T, Kothari M, Paul P, Jacob P, Thomas R. Intracameral amphotericin B injection in the management of deep keratomycosis. *Cornea*. 2002 Oct;21(7): 653–656.